LETTER

Treatments for macular degeneration: summarising evidence using network meta-analysis

In studying treatments for age-related macular degeneration (AMD), randomised controlled trials have typically used placebo or verteporfin in the control group. Hence, information on direct head-to-head comparisons between the newest agents is still needed.

Network meta-analysis (NMA) is a tool that summarises the information on comparative effectiveness when three or more treatments are proposed for the same clinical indication. NMA includes both direct comparisons (based on real trials) and indirect comparisons (based on statistical testing in the absence of a real head-to-head trial). The main advantage of NMA lies in its communicative value; another advantage is that it overcomes one limit of traditional meta-analysis wherein only comparisons between two treatments can be considered. Its main disadvantage is related to the indirect nature of the statistical comparisons not based on real clinical trials; in fact, the 'indirect' results are essentially derived from the transitive property (if A is much better than B and C is better than B, then A is assumed to be better than C) in which appropriate statistical thresholds are, however, incorporated.

We conducted a simplified NMA to examine all controlled trials evaluating treatments for AMD. First, a PubMed search (on 20 April 2011) identified five controlled studies (acronyms: ANCHOR, FOCUS, MARINA, VISION, ABC) that shared the endpoint of the loss of fewer than 15 letters on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at 1 year. These data of comparative effectiveness were then incorporated into a simplified graph (figure 1A). Our analysis indicated that the indirect comparison between ranibizumab and bevacizumab showed no significant difference in this endpoint.

More recently, the preliminary results of the CATT trial have been made available. Figure 1B shows how the graph is rearranged if the indirect comparison between ranibizumab and bevacizumab is replaced by a direct one based on the results of the CATT trial. Interestingly, the findings of NMA in figure 1A are in full agreement with those in figure 1B. Hence, the new 'real' trial confirms the 'indirect' results previously predicted by NMA.

In conclusion, the current information on effectiveness, interpreted according to NMA, indicates that anti-vascular endothelial growth factor (VEGF) agents can significantly improve the outcome of patients with AMD. Ranibizumab and bevacizumab show no difference in effectiveness, but the latter agent is much less expensive than the former.

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Figure 1 Network meta-analysis (NMA) of treatments for age-related macular degeneration (AMD). The two graphs show the same analysis carried out before (A) and after (B) the publication of the CATT study. In both graphs, each direct comparison is represented by a solid line and each indirect comparison by a dotted line; statistical results are given as RR with 95% CI; the endpoint is the proportion of patients losing less than 15 letters of visual acuity in the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. All primary data were extracted from the studies by Tufail et al and by the CATT group, and from references 5, 8, 9 and 10 of the article by Takeda et al. Symbols = denotes comparisons showing no difference; + indicates which treatment is favoured at levels of statistical significance, and vice versa; ‘t’ indicates the same in the absence of statistical significance. Details on the trial-specific event rates can be accessed as supplementary material online and at www.osservatorioinnovazione.org/netma/bjo_fadda2011.pdf.
REFERENCES


